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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,128	06/03/2008	Norman James Maitland	100846.59603US	5914

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,128	MAITLAND ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendment filed on 9/15/06 canceled claims 22-74. Claims 1-21 are currently pending and under examination. An action on the merits follows.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 9/15/06 is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the information disclosure statement has been considered by the examiner, and an initialed and signed copy of the 1449 is attached to this action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, and 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is further noted that claims 1-2, and 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 1, the independent claim, recites a method for the isolation of prostate stem cells comprising the selective

enrichment of prostate stem cells which express CD133 antigen. However, as written, this limitation does not contain any specific active method step which results in the isolation or enrichment of cells which express CD133 antigen. The method as written omits a recitation of any starting population of cells from which the prostate stem cells are to be isolated/enriched, and further fails to include any specific step for achieving the desired isolation/enrichment. As such, the method claim is indefinite as the metes and bounds of the claim cannot be determined and appears to omit essential steps required to isolate prostate stem cells as claimed. Claims 2, and 12-14 depend on claim 1 and thus are included in this rejection.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 depends on claim 3, and further recites additional steps identified as " i)" and "ii)". Step (ii) of claim 4 recites "passaging the selected cells in (i) in a serum free medium". Since both claim 4 and claim 3 upon which claim 4 depends contain a step (i), it is unclear which cells are to be passaged. Further, there is no antecedent basis for "the selected cells" in either the step (i) of claim 3 or the step (i) of claim 4. Note that step (i) of claim 4 does not indicate that the cells which express CD133 antigen are in fact the bound cells selected in step (iii) of claim 3. As such, the metes and bounds of the claimed method cannot be determined.

Claims 15-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 15, upon which claims 16-21 depend, recites a cell culture of

"substantially" pure prostate stem cells. However, the term "substantially" is a relative term such that it is unclear what percentage of cells within the cell culture must be prostate stem cells in order to qualify as a cell culture of "substantially" pure prostate stem cells. These, the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 11-12, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins et al. (2001), J. Cell Science, Vol. 114, 3865-3872.

Collins et al. teaches a method for isolating an enriched population of prostate stem cells comprising 1) providing a cell preparation comprising prostate stem cells by digesting human prostate tissue with collagenase, and isolating basal epithelial cells within the stromal population through immunomagnetic positive selection of CD44 expressing cells, and 2) enrichment of prostate stem cells from the CD44 positive basal cell population through selection of cells which rapidly adhere to dishes coated with collagen type I (Collins et al., page 3866 and 3868). Collins et al. teaches that rapidly adhering CD44+ cells are further $\alpha 2\beta 1$ integrin bright, and are capable of differentiating into prostate glandular tissue including the generation of acini (Collins et al.,

page 3869). Please note that the method steps taught by Collins et al. are identical to those recited in independent claim 3.

While Collins et al. does not test the rapidly adhering CD44+ $\alpha 2\beta 1$ integrin + prostate stem cells for the expression of the CD133 antigen or human epithelial antigen (also known in the art as Ep-CAM), the expression of CD133 antigen and human epithelial antigen by these prostate stem cells is an inherent characteristic of prostate stem cells isolated using the Collins et al. method, which as noted above is the exact same method as recited in claim 3.

The applicant is reminded that it is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff*, 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed.Cir. 1990); *In re Swinehart*, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Further, case law states that "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or *In re Best*, 195 USPQ 430, 433 (CCPA 1997). In addition, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Finally, the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the

claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989).

Therefore, by teaching an enriched rapidly adhering CD44+ $\alpha 2\beta 1$ integrin + prostate stem cell population isolated using the exact method steps set forth in the claims as written, Collins et al. anticipates the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-10, 13-14, and 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (2001), J. Cell Science, Vol. 114, 3865-3872, in view of US Patent Application Publication 2007/0134794 (published 2007, with an effective filing date of 10/15/01), hereafter referred to as Mangano.

Collins et al. teaches a method for isolating an enriched population of prostate stem cells comprising 1) providing a cell preparation comprising prostate stem cells by digesting human prostate tissue with collagenase, and isolating basal epithelial cells within the stromal population through immunomagnetic positive selection of CD44 expressing cells, and 2) enrichment of prostate stem cells from the CD44 positive basal cell population through selection of cells which rapidly adhere to dishes coated with collagen type I (Collins et al., page 3866 and 3868). Collins et al. teaches that rapidly adhering CD44+ cells are further $\alpha 2\beta 1$ integrin bright, and are capable of differentiating into prostate glandular tissue including the generation of acini (Collins et al., page 3869). Please note that the method steps taught by Collins et al. are identical to those recited in independent claim 3.

While Collins et al. does not test the rapidly adhering CD44+ $\alpha 2\beta 1$ integrin + prostate stem cells for the expression of the CD133 antigen or human epithelial antigen (also known in the art as Ep-CAM), the expression of CD133 antigen and human epithelial antigen by these prostate stem cells is an inherent characteristic of prostate stem cells isolated using the Collins et al. method, which as noted above is the exact same method as recited in claim 3. The applicant is also reminded that reliance upon inherency is not improper even though rejection is based on Section 103 instead of Section 102. *In re Skoner.* 186 USPQ 80 (CCPA).As stated in MPEP 2112, the express, implicit, and inherent disclosures of a prior art reference may be relied upon in

the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." In *re Napier,* 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995). See also *In re Grasselli,* 713 F.2d 731,739, 218 USPQ 769, 775 (Fed. Cir. 1983).

Collins et al. differs from the instant methods and cell cultures as claimed by not teaching to isolate prostate stem cells from cancerous prostate tissue, either primary prostate tumor tissue, or metastatic tissue. Collins et al. also does not specifically teach a prostate cancer stem cell. However, at the time of filing, Mangano teaches methods for selecting and enriching for stem cells, in particular cancer stem cells, from various tissues and organs, and cultures of the selected stem cells or cancer stem cells (Mangano et al., paragraphs 6-8, 12-13). Mangano et al. further teaches that epithelial stem cells and other stem cells transform into cancer stem cells and are associated with cancers such as prostate cancer (Mangano et al., paragraph 44). Mangano et al. also teaches that it is to be expected that cancer stem cells would express stem cell markers of the original stem cell (Mangano et al., paragraph 46). More specifically, Mangano et al. teaches to select and isolate prostate stem cells and prostate cancer stem cells from such sources as solid tumors or metastatic tissue (Mangano et al., paragraphs 37, 40, 44, 46, 60, and 63). Finally, Mangano et al. teaches that cancer stem cells can be differentiated from non-cancerous stem cells by their ability to form tumors in a host (Mangano et al., paragraphs 37 and 104).

Therefore, based on the motivation provided by Mangano et al. to select and enrich for prostate stem cells or prostate cancer stem cells from source tissue which is a solid tumor or metastatic tissue, and the further teachings of Mangano et al. that cancer stem cells, including prostate cancer stem cells, share similar marker protein expression as the original stem cell, it

would have been *prima facie* obvious to the skilled artisan at the time of filing to practice the methods for selecting prostate stem cells taught by Collins et al. using primary prostate tumor tissue or metastatic prostate cancer tissue as the tissue source for isolating the stem cells, or alternatively it would have been *prima facie* obvious to the skilled artisan at the time of filing to select and enrich for prostate cancer stem cells using the methods for selecting prostate stem cells taught by Collins et al. The skilled artisan would further have had a reasonable expectation of success in isolating either prostate stem cells or prostate cancer stem cells from prostate tumor tissue or metastases using the Collins method of selecting for CD44+ cells, and further selecting for cells that rapidly adhere to collagen I (i.e. express high levels of $\alpha 2\beta 1$ integrin) since Mangano et al. teaches that both stem cells and cancer stem cells can be found in tumors and metastases, that cancer stem cells would be expected to express the same markers used for stem cell selection, and that stem cells versus cancer stem cells can be differentiated by their ability to form tumors in animals.

Regarding the expression of AC133 antigen and human epithelial antigen on the cancer stem cells, while neither Collins et al. nor Mangano teach that prostate cancer stem cells express these markers, the expression of both AC133 and human epithelial antigen are considered to be an inherent characteristic of prostate cancer stem cells isolated using the Collins et al. method, which as noted above is the exact same method as recited in claim 3. The office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than

those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989).

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633